



Request for Proposal (RFP) for Ethical, Social, Cultural, and Regulatory Considerations for Human Gut Microbiome-based interventions

1. RFP Background & Objectives

The gut microbiome describes communities of microorganisms found within the gastrointestinal (GI) tract, including bacteria but also archaea, fungi and viruses. A growing body of research has demonstrated how the composition of the human gut microbiome can impact or contribute to a range of health conditions – including diarrheal diseases, mental health conditions via the gut-brain axis, and inflammatory and infectious diseases via effects on the immune system. Additionally, the microbiome can also impact response to therapeutics and vaccines.

As we continue to develop the evidence and our understanding of how the microbiome impacts both causal pathways to disease and response to biomedical interventions, there is growing potential for microbiome-based interventions and therapies to address key health challenges. Microbiome-based therapies include: dietary interventions, prebiotics, probiotics, antibiotics, phage therapy, faecal microbiota transplantation (FMT), live biotherapeutics and microbiome mimetics. There may also be important applications for diagnostic indicators, for instance in the mental health space.

Yet, as a new class of health interventions—for which there are not always clear or consistent pathways, evidence standards, and oversight to reach the market and end users—there are a number of questions about the relevant ethical, social, and cultural considerations surrounding their development, approval, and introduction. Moreover, the route to market approval may have important implications for social understanding, acceptance, and uptake of the products—as well as equity in access, appropriate use, and distribution of potential benefits and/or risks.

This work will produce insights on the ethical, social, and cultural considerations for the development and introduction of gut microbiome-targeted interventions. It will also entail an assessment of possible regulatory pathways, to illuminate the interplay between various ethical, social, and cultural implications and different routes to market authorization and oversight.

Key outputs will include:

- A report detailing ethical, social, and cultural considerations relevant to the development, approval, and introduction of gut microbiome-based interventions, with specific examples of how these may differ across contexts, population subgroups, for different types of microbiome-based interventions and classifications, and for different health conditions and targets.
- Review and synthesis of the relevant literature, policy documents, and regulatory instruments related to market authorisation pathways of gut microbiome-based products, with in-depth analysis across 6-8 settings/jurisdictions (e.g., UK, USA, EU, India, Bangladesh, South Africa, Kenya, Japan, etc.)



- Assessment reflecting how ethical, social, and cultural considerations should inform options for regulatory pathways to market – and conversely how routes to market authorisation and corresponding oversight may have ethical, social, and cultural implications for gut microbiome-based products.

2. RFP Specification

Scope and Exclusions

Although there are a range of microbiomes relevant to health, this commissioned research will focus exclusively on products related to the *gut microbiome*. These products include: prebiotics, probiotics, synbiotics, antibiotics, phage therapy, faecal microbiota transplantation (FMT), live biotherapeutics and microbiome mimetics. For any therapeutic products, the focus should be on interventions with a specific health claim or indication, rather than those promoting general wellness.

This work will also cover applications of gut microbiome diagnostic approaches, including development of predictive microbiome-based biomarkers that may enable identification of certain risk factors and earlier detection of conditions like depression, anxiety disorders, cancers, etc. – as well as stratification of patients to treatment courses best suited to them. To the extent that it is relevant, there may also be value in exploring the burgeoning field of direct-to-consumer, at-home microbiome test kits to understand various ethical, social, and cultural considerations—and the context into which novel clinical diagnostic tests may be introduced.

Because of the novelty of these products, there could be some settings where there are no precedents or available documents specific to microbiome-based products. In these settings, there may be useful analogous examples to draw upon, like supplements, food additives, herbal remedies, or other products to provide insights on potential ethical, social, cultural, and regulatory considerations. Review of these products across settings can also shed light on ethical, cultural, and social considerations for microbiome-based products that are not classified as medicinal products nor held to the same stringent regulatory guidance for efficacy and safety. As and when these examples feature, the supplier should indicate specifically how these inform the context of future microbiome-based products.

The overarching research questions for this work are:

- I. **What are the key ethical, social, and cultural considerations that should inform the development, evaluation, introduction, and oversight of gut microbiome-based products?**
 - How might these differ for various kinds of products, based on the setting, the classification of the product, the health condition of interest, and the intended use and benefit (e.g., diagnosis, personalised/precision medicine, co-administration with standard therapy, standalone use, prevention vs. treatment applications, etc.)?
 - How should these considerations inform the development of appropriate studies, evidence standards, and regulatory pathways for these products?



II. What are the current and potential future regulatory mechanisms and pathways by which these products could approved for market authorisation and/or distribution? How should appropriate routes be informed by relevant ethical, social, and cultural considerations? Elements of this work should include:

- Classification of products as a drug, supplement, food, live biotherapeutic products, or other, alongside any other relevant considerations for borderline medicinal products
- Required evidence and assurances in support of market authorisation, including for efficacy, selection of study endpoints, and safety, as well as compliance with various standards like GCP and GMP.
- Associated pharmacovigilance, screening, and post-market requirements
- Implications for equity in access (e.g., Rx requirements, coverage via public insurers or programmes)

III. How might different routes to market for microbiome-based products influence or impact important social, cultural, and ethical dimensions? These include but are not limited to:

- Public understanding, perceptions, acceptance, and uptake of products
- Trust in health agencies and regulatory bodies
- Potential distributions of associated harms and benefits of these products
- Implications for innovation for health conditions with unmet or under-met needs, and equity in R&D investment to address different burdens of disease
- Implications for the wider market of microbiome-based products, and the interplay between commercial products that do not go through clinical research pathways vs. those with more robust evidence and stringent oversight
- Implications for distribution channels, access to and affordability of microbiome-based products that have health benefits

Some broad categories regarding the kinds of ethical, social, and cultural considerations that this exercise should surface include (but are not limited to):

- Appropriate assessment of benefits and risks of these products, and appropriate study design to understand net benefits/harms, non-inferiority, interaction affects, etc.
- Implications for explanatory models of health conditions, including how this may affect perceptions of personal responsibility, stigma, sense of self, biological vs social drivers of various kinds of ill health.
- Implications of diagnostics (including direct-to-consumer approaches), questions of validity, predictive value, and interpretation of findings, as well appropriate connection to care and services.
- Contribution of microbiome-based products to health inequities (e.g., when applied for precision medicine and stratification purposes against a background context of inequitable access; when developed in an HIC context and not transferable to other settings due to technological barriers or mismatch of microbiota, etc.)



- Issues related to big data mining of gut microbiota and nuanced implications for privacy given symbiotic relationship with human host that go beyond standard issues for biobanking.
- How classification and perception of products as “lifestyle” vs “medicinal” interventions may have implications for attitudes, acceptance, uptake – and potential implicit commentary about diet and lifestyles of various cultural groups.

Please note: *proposals may be submitted addressing just the ethical, social, and cultural considerations or just the regulatory science aspects and we may elect to commission more than one supplier to deliver the full package of work. In the event that we commission multiple suppliers, we would hold a convening workshop to generate insights on the interplay between these two areas, and expect the suppliers to collaboratively contribute to final outputs that draw the links between regulatory pathways and ethical, social, and cultural implications.*

Deliverables:

- Inception report detailing the scope, methodological approach(es), timetable, and related activities.
- Participation and presentation of early findings in a Wellcome workshop in September 2024 on microbiome research and interventions.
- An interim report detailing ethical, social, and cultural considerations relevant to the development, approval and introduction of gut microbiome-base interventions, with specific examples of how these may differ across contexts, for different types of microbiome-based interventions, and with different health targets. This may include:
 - Review and synthesis of the literature, case studies relevant to different types of health conditions, case studies for different uses (e.g., diagnostic, therapeutic, co-administration), primary data collection related to attitudes and perceptions of microbiome-based products in select settings, etc.
- An interim regulatory science report detailing market authorisation pathways of microbiome-based products, with select case studies across 6-8 geographically varied national settings (e.g., UK, USA, EU, India, Bangladesh, South Africa, Kenya, Japan, etc.). This may include:
 - Literature and policy document review and synthesis; primary interviews and consultations with representatives from regulatory agencies
 - Where there is no precedent, available documents, or activities in development specific to microbiome-based products, suppliers may draw upon examples of supplements, food additives, and other products that may provide insights on potential options for regulatory mechanisms relevant to MBPs.
- Participation in activities to crosswalk findings from ethics work package with the potential regulatory pathways to understand how different evidence standards on safety & efficacy, approval routes and oversight mechanisms interplay with social, cultural, and ethics implications, including as related to potential understanding,



attitudes, acceptance and uptake [this may include an in-person and/or virtual meetings amongst selected suppliers]

- Development of a final in-depth report synthesising findings and insights for internal use, with at least 1 round of feedback and revisions, and a presentation of findings to Wellcome staff.
- Development of a public-facing summary outlining key findings for internal and external audiences.

Timeline for these deliverables is as follows:

Deliverable	Month of Completion
Inception report	First 6 weeks
Materials and Participation in Workshop	Month 3
Interim report detailing ethical, social, and cultural considerations	Month 5
Interim regulatory science report	Month 5
Participation in activities linking up regulatory pathways and ethical, social, cultural aspects	Month 7
Final in-depth report synthesising findings and insights	Month 9
Public-facing summary	Month 9
Supplier Presentations to Wellcome	Month 10

3. RFP Timetable

#	Activity	Responsibility	Date
1	RFP issue to Suppliers AND/OR [RFP issued on Contract Opportunities webpage	Wellcome	24 January 2024
2	Submission of Expression of Interest and Supplier Q&A	Supplier	06 February 2024
3	Return of Supplier Q&A to Suppliers	Wellcome	13 February 2024
4	Submission of RFP Response	Supplier	04 March 2024
5	RFP Evaluation Period	Wellcome	05 March 2024 to 15 March 2024
6	Supplier Presentations	Supplier	20 March 2024 to 05 April 2024
7	Notification of Contract Award	Wellcome	w/c 08 April 2024
8	Contract Negotiation	Wellcome & Supplier	April 2024
9	Contract Start Date	Wellcome & Supplier	May 2024



4. Response Format

The following headers support the timetable by providing further detail of the key steps.

Expression of Interest and Supplier Q&A

Suppliers are asked to submit a short expression of interest by e-mail to the Wellcome contact in accordance with the RFP timetable, which should contain the following information.

- Which of the two RFP areas they are submitting a proposal for. (Analysis of Regulatory Pathways; Analysis of ethical, social and cultural aspects of developing and introducing these products).
- Confirming whether you are an organisation or individual.
- If an organisation, please provide registered name, address, and registration number.
- A non-binding cost estimate, as a single figure in GBP
- Any questions you have about the exercise and activity.

Prior to the submission of your full proposal to the RFP, Suppliers are provided the opportunity to submit any questions they have about the exercise and the activity. All questions will be collated, anonymised, answered and returned to all Suppliers who have submitted an expression of interest in the RFP process. Please make sure you ask all questions at this stage. Once Wellcome have responded to all questions if you have any additional questions after this deadline these will not be answered to ensure that this is a fair and equitable process.

Submitting an EOI/Q&A is not a binding commitment to submit a full proposal should your organisational priorities change, you will not then be penalised for future opportunities

Please note, if we have an overwhelming response, we may choose to use this EOI stage as a selective phase, this is at Wellcome's discretion.

RFP Response

Suppliers should make clear which of the two areas below they are submitting a proposal for. You can submit a proposal for just one or both areas.

- *Analysis of Regulatory Pathways for Gut Microbiome-based products*
- *Analysis of ethics considerations and social and cultural aspects of researching and introducing products*

Suppliers may need to work with other stakeholders at Wellcome's request.



Suppliers submitting a full proposal should cover the following areas in their response:

#	Question	Max (Words)
Experience		
1.	<p>Provide an overview of your experience in the area and whether/how you will work with any external experts or partners to cover the gaps in your knowledge.</p> <p>Include any relevant experience completing ethics research, regulatory science and policy analysis, comparative case studies, and/or landscaping analyses. Also include any relevant background related to microbiome-based research or other borderline medicinal products.</p>	500
2.	<p>Provide evidence of your track record, including specific case studies of where you have successfully provided similar services to those described in this RFP.</p>	500
Approach		
3.	<p>Detail your methodology for completing the analyses, including:</p> <ul style="list-style-type: none"> • The approach and methods • Proposed project plan including timelines • Management plan, including role of team members • Plan for engagement with Wellcome during contract • Plan for production of deliverables and final report, including any copy editing, formatting and graphics • Diversity and inclusion planning (how you will ensure that the work and synthesis appropriately reflect perspectives of different groups of people) 	2000
4.	<p>Highlight any risks or challenges you foresee in meeting the requirements of this RFP, along with any proposed mitigations. Please present this as a table.</p>	200
5.	<p>Provide an overview of the stages and timeframes in which you propose to meet the RFP requirements (for example, as a Gantt chart).</p>	N/A
Budget		
6.	<p>Provide a detailed budget including all costs and expenses, specifying all day rates of individuals involved, the allocation 300 words Page 7 of 10 Sensors for Mental Health RFP of days between members of the team, and the cost of activities. The budget must include allocation of funds for at least two senior academic consultants/senior research software engineers.</p>	300



Evaluation Criteria

Criteria	Detail	%
Approach	<p><i>Coverage:</i> How well are the desired focus areas (as outlined in the specification) covered in the proposed methodology address?</p> <p><i>Quality:</i> Is the proposed methodology aligned with our needs?</p> <p><i>Utility:</i> Will the proposed methodology deliver the desired, credible, and useful results?</p> <p><i>EDI:</i> Has the approach appropriately accounted for equity, diversity and inclusion in it's conception, design, and planned implementation?</p>	50%
Experience	<p><i>Skills and Experience:</i> Does the supplier have the relevant skills, experience, and contextual understanding to deliver this work?</p>	30%
Delivery & Outputs	<p><i>Communication:</i> Is there a good plan for communicating with the Wellcome team?</p> <p><i>Delivery plan:</i> Is the proposed delivery plan appropriate and achievable?</p> <p><i>Feasibility:</i> How feasible is the delivery plan? Are there significant risks associated with the proposed timelines, and how well are they mitigated?</p>	10%
Budget	<p><i>Value for Money:</i> Is the proposed work adequately budgeted and does it represent good value for money?</p>	10%
Total:		100%

Contract Feedback

This section allows Suppliers to provide specific feedback to the contractual agreement which will be used should their proposal be successful. This is the suppliers' opportunity to provide negotiation points on Wellcome's terms and conditions. We will not consider negotiations that are raised in your response to this proposal i.e. after the contract has been awarded so as not to delay the contracting process. Please ensure you engage with a relevant legal contact if applicable. Contract feedback is to be incorporated into your proposal as an annex and in the following format;

Clause #	Issue	Proposed Solution/Comment

Suppliers submitting proposals as a registered company should review Wellcome's Standard terms and Conditions [document](#).

Individuals submitting proposals as a sole trader (not registered) should review this [document](#).



Individuals submitting proposals through their own personal services company please highlight this to the Wellcome contact immediately (see point 6 below).

Information Governance

Wellcome is committed to upholding data protection principles and protecting your information. The [Wellcome-Privacy-Statement-2023.pdf](#) explains how, and on what legal basis, we collect, store, and use personal information about you. This includes any information you provide in relation to this proposal.

Under [GDPR/Data Protection law](#), Wellcome must keep a record of all personal information it is processing (i.e., collecting, using, and sharing). This record will be made available to the Information Commissioner's Office upon request.

This is Wellcome's record of data processing activities which meets GDPR article 30 requirements.

Suppliers will be asked to complete the [TPSRA2](#) assessment before presentation stage to assess how you handle data.

Supplier Presentations

Following a submission of the proposal successful proposals will be invited to a virtual meeting which will last 50 minutes in total and will be a PowerPoint presentation followed by questions and answers session.

5. About Wellcome

Wellcome improves health for everyone by funding research, leading policy and advocacy campaigns, and building global partnerships. Collaborative research that involves a diverse range of people from different fields of interest is key to progress in health science – and to achieving our aim of fostering a healthier, happier, world. We're taking on the biggest health challenges facing humanity – climate and health, infectious disease, and mental health – to find urgent solutions and accelerate preventions. Find out more about Wellcome and our work at: [wellcome.org](https://www.wellcome.org).

6. Prospective Suppliers Personnel - IR35 and Off Payroll Working Rules

Before the RFP response deadline, Prospective Suppliers must make the Wellcome Contact aware if they are intending to submit a proposal where the services will be provided by any individuals who are engaged by the Prospective Supplier via an intermediary i.e.

- Where the Prospective Supplier is an individual contracting through their own personal services company; or
- The Prospective Supplier is providing individuals engaged through intermediaries, for the purposes of the IR35 off-payroll working rules.



7. Equity Diversity and Inclusion

Embracing [diversity and inclusion](#) is fundamental to delivering our mission to improve health, and we are committed to cultivating a fair and healthy environment for the people who work here and those we work with. We want to cultivate an inclusive and diverse culture, and as we learn more about barriers that disadvantage certain groups from progressing in our workplace, we will remove them.

Wellcome takes diversity and inclusion seriously, and we want to partner with suppliers who share our commitment. We may ask you questions related to D&I as part of our RFP processes.

8. Disability Confident

The Wellcome Trust is proud to be a Disability Confident Employer (DC Level 2) and we encourage all our partners and suppliers to do the same. More information about this can be found on the government website [Disability Confident employer scheme and guidance - GOV.UK \(www.gov.uk\)](#). Disability Confident is creating a movement of change, encouraging employers to think differently about disability and take action to improve how they recruit, retain and develop disabled people.

9. Accessibility

Wellcome is committed to ensuring that our RFP exercises are accessible to everyone. If you have a disability or a chronic health condition, we can offer adjustments to the response format e.g., submitting your response in an alternate format. For support during the RFP exercise, contact the Wellcome Contact.

If, within the proposed outputs of this RFP exercise, specific adjustments are required by you or your team which incur additional cost then outline them clearly within your commercial response. Wellcome is committed to evaluating all proposals fairly and will ensure any proposed adjustment costs sit outside the commercial evaluation.

10. Independent Proposal

By submission of a proposal, prospective Suppliers warrant that the prices in the proposal have been arrived at independently, without consultation, communication, agreement or understanding for the purpose of restricting competition, as to any matter relating to such prices, with any other potential supplier or with any competitor.

11. Funding

For the avoidance of doubt, the output of this RFP exercise will be funded as a **Contract** and not as a Grant.



12. Costs Incurred by Prospective Suppliers

It should be noted that this document relates to a Request for Proposal only and not a firm commitment from Wellcome to enter into a contractual agreement. In addition, Wellcome will not be held responsible for any costs associated with the production of a response to this Request for Proposal.

13. Sustainability

Wellcome is committed to procuring sustainable, ethical and responsibly sourced materials, goods and services. This means Wellcome seeks to purchase goods and services that minimise negative and enhance positive impacts on the environment and society locally, regionally and globally. To ensure Wellcome's business is conducted ethically and sustainably, we expect our suppliers, and their supply chains, to adhere to these principles in a responsible manner.

14. Wellcome Contact Details

The single point of contact within this RFP exercise for all communications is as indicated below;

Name: Alyce O'Connor
Pronouns: She/Her
Role: Procurement Officer
Email: contracts@wellcome.org